

**REMARKS/ARGUMENTS**

Claims 1-63 are pending in the present application. Claims 3, 4, 7, 8, 18-20, 23-24, 26, 29-34, 36-40, 44-45 and 52-63 were previously withdrawn from consideration as drawn to a non-elected invention. Claims 2, 6, 9, 15, 16, 22, 42, 43, 47, 48, and 49, under consideration, have been amended for clarity or punctuation. Withdrawn claims 7, 8, 56, 57, 62 and 63 have been amended for clarity or punctuation. New claims 64-72 have been added which Applicants believe fall within the elected invention. Support for new claims 64-68 can be found throughout the specification. Support for new claim 69 can be found at least at page 6, lines 22-23. Support for new claims 70-72 can be found at least at page 14, lines 18-24 and page 22, lines 1-4. Accordingly, claims 1, 2, 5, 6, 9-17, 21, 22, 25, 27, 28, 35, 41-43, 46-51, and 64-72 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any subject matter of the claims as previously presented.

Applicants request rejoinder of methods claims to the extent they incorporate all the limitations of allowed composition claims. In re Ochiai.

**Drawings**

Applicants acknowledge approval of the new Figure 8.

**Concerning Rejections Under 35 U.S.C. 112, first paragraph**

Applicants acknowledge the Examiner's withdrawal of the rejection under 35 U.S.C. 112, first paragraph.

The Examiner states that not all references cited by Applicants have been listed on a 1449 form and therefore have not been considered. Applicants believe that all references cited in the Amendment and the Tikoo Declaration submitted on June 10, 2003 have been submitted to the USPTO. In particular, Akalu et al.; Colby et al.; Fields Virology, 1991; Fields (Horowitz) Fundamental Virology, 1991 ; Reddy et al. 1999; Mathias et al.; and Vigne et al. were submitted to

the USPTO in the Supplemental Information Disclosure Statement (IDS) mailed June 10, 2003 (and returned initialed by the Examiner indicating her consideration).

Zheng et al.; Mittal et al.; and Reddy et al., 1998, were submitted to the USPTO in the IDS mailed August 30, 2001 (and returned initialed by the Examiner indicating her consideration).

### **Concerning Rejections Under 35 U.S.C. 103(a)**

1. The Examiner maintains the rejection of claims 1, 2, 5, 6, 9-11, 14-17, 21, 22, 27, 28, 35, 41, 42, 43, 46-49, and 51 as allegedly unpatentable over Mittal, et al. (U.S. Pat. No. 5,820,868, 1998, see IDS Paper No. 3), Krasnykh, et al. (Journal of Virology, 1996, see IDS Paper No. 3) and Reddy, et al. (Journal of Virology, 1999, see IDS Paper No. 3).

Applicants traverse this rejection of claims. Applicants do not agree or concede that a *prima facie* case of obviousness has been established and submit that the invention is non-obvious in view of the cited references. In order to establish a *prima facie* case of obviousness, there has to be, *inter alia*, some motivation or suggestion provided by the references, or in combination with the knowledge available to the skilled artisan, to modify the art cited or to combine reference teachings. Applicants submit that there is no motivation to combine references.

Applicants are submitting concurrently herewith a Declaration Under 37 CFR 1.132 establishing that the cited Reddy, et al. 1999 reference describes the work of inventors. This Declaration removes Reddy et al. as a reference under 35 USC §102(a). See MPEP 715.01(c) and In re Katz, 215 USPQ 14 (CCPA 1982).

The Examiner cites Mittal et al. and states that they disclose production of a recombinant bovine adenovirus for production of foreign proteins. The Examiner states that Mittal et al. teach the cloning and sequencing of the BAV E3 region and fiber region. The Examiner in the Office Action mailed December 10, 2002 concludes that Mittal et al. do not teach inserting a heterologous sequence into the fiber region or modifying the fiber region of a bovine adenovirus in order to alter the tropism of the virus. The Examiner cites Krasnykh et al. and states that they teach the modification and alteration of adenoviral fiber protein in order to alter viral tropism. Krasnykh et al.

describe a two plasmid system that allows for generation of human adenovirus vectors containing variant adenovirus fiber. See Krasnykh, the Abstract. The Examiner in the Office Action mailed December 10, 2002 concludes that Krasnykh et al. do not teach modifying tropism of a bovine adenovirus.

Applicants submit that there is no motivation provided in either of Mittal et al. or Krasnykh et al. to combine references. There is no suggestion to combine Mittal et al., which the Examiner states do not teach altering tropism of the adenovirus by modifying the fiber region, with Krasnykh et al., which the Examiner states do not teach modifying tropism of a bovine adenovirus.

Furthermore, in determining obviousness, Section 103 expressly requires considering the claimed invention "as a whole". The properties and advantages of the invention are part of the invention as a whole. As described in the Suresh K. Tikoo Declaration submitted with the amendment mailed June 10, 2003, a bovine adenovirus that comprises nucleic acid encoding a HAV-5 fiber knob region fused to the BAV-3 tail and shaft, one illustrative example encompassed within the invention, is unexpectedly able to transduce non-human mammalian cell lines. This unexpected property of a bovine adenovirus vector comprising a human fiber region is not taught, suggested or appreciated by either of Mittal et al. or Krasnykh et al., taken alone or in combination.

Applicants submit that there is no motivation to combine the references cited by the Examiner. As concluded by the Examiner, Mittal et al. do not teach altering tropism of the bovine adenovirus by modifying the fiber region and Krasnykh et al. do not teach modifying tropism of a bovine adenovirus. Therefore, Applicants submit that when the invention is viewed as a whole, this obviousness rejection must fail as a matter of law. Applicant request withdrawal of this Section 103 rejection of claims.

2. The Examiner maintains the rejection of claims 1, 2, 5, 6, 9-17, 21, 22, 27, 28, 35, 41, 42, 43 and 46-51 under 35 U.S.C. § 103(a) as allegedly unpatentable over Romanczuk et al. (WO 99/36545, see IDS Paper No. 3) and Reddy et al. (Journal of Virology, 1999, see IDS Paper No. 3).

Applicants traverse this rejection of claims.

Applicants are submitting concurrently herewith a Declaration Under 37 CFR 1.132 establishing that the cited Reddy, et al. reference describes the work of inventors. This Declaration removes Reddy et al. as a reference under 35 USC §102(a). See MPEP 715.01(c) and In re Katz, 215 USPQ 14 (CCPA 1982).

The Examiner states that Romanczuk et al. teach the production of chimeric adenovirus vector by modifying the capsid protein with the heterologous ligand to improve or alter the infectious capability of the vector. The Examiner concludes in the Office Action mailed December 10, 2002 that Romanczuk et al. describe human adenovirus and that there are no teachings in Romanczuk et al. regarding bovine adenovirus, much less the presently claimed bovine adenovirus comprising a modification in a polynucleotide encoding a capsid protein.

In the present Office Action, the Examiner states that "one having ordinary skill in the art would have been motivated to utilize a bovine adenovirus as a vaccine vector because the average human population would not have produced neutralizing antibodies to bovine adenovirus as this virus would not normally infect the population", yet the Examiner does not provide any evidence or citation to support this allegation. The Examiner also alleges that utilizing a bovine adenovirus vector as a vaccine vector would reduce the risk of recombination with wild type viral sequences creating a replication competent virus. The Examiner does not provide any evidence or citation to support this allegation. The Examiner alleges that utilizing BAV type 1 and 2 would allow for multiple vaccination with a bovine adenovirus vector as the subject would not have made neutralizing antibodies to the particular vectors. The Examiner does not provide any evidence or citation to support the allegations. In order to support an obviousness rejection, the teachings or suggestions, as well as the expectation of success, must come from the art cited and not Applicants' disclosure. General conclusions concerning what is "basic knowledge" or "common sense" to one of ordinary skill in the art without specific factual findings and concrete evidence in the record to support these findings will not support an obviousness rejection. See In re Lee, 277 F.3d 1338, 1345 61 USPQ 2d 1430, 1434-35 (Fed. Cir. 2002).

Applicants submit that the Examiner has not met her burden of making a *prima facie* case of obviousness. Furthermore, when taken as a whole, the presently claimed invention is not rendered

obvious by the art cited by the Examiner. In view of the evidence and arguments of record,

Applicants respectfully request withdrawal of the Section 103 rejections of claims.

**CONCLUSION**

Applicants have, by way of the amendments and remarks presented herein, made a sincere effort to overcome rejections and address all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant(s) petition(s) for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 293102003000. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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